UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,225	09/17/2003	Se-Jin Lee	JHU1220-6	8745

7590 05/25/2006

Lisa A. Haile, J.D., Ph.D.
GRAY CARY WARE & FREIDENRICH LLP
Suite 1100
4365 Executive Drive
San Diego, CA 92121-2133

EXAMINER	
MERTZ, PREMA MARIA	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/666,225	LEE ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,8,9,12,15-18,23-29 and 37* is/are pending in the application.

4a) Of the above claim(s) *1-4, 6, 8-9, 12, 23-29, 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Amended claims 15-16 (4/7/2006) and original claims 17-18 are under consideration by the Examiner.

2. Receipt of applicant's arguments and amendments filed on 4/7/2006 is acknowledged.

3. The following previous objections and rejections are withdrawn in light of applicants amendments filed on 4/7/2006:

(i) the rejection of claims 15-18 under 35 USC 112, second paragraph.

Applicant's arguments with respect to claims 15-18 have been considered but are moot in view of the new ground(s) of rejection.

4. The objection to the title of the invention is being maintained for reasons of record set forth at page 2 of the previous Office action (12/5/2005) because Applicants have failed to amend the title to reflect the method being claimed.

5. Applicant's arguments filed on 4/7/2006 have been fully considered and were persuasive in part. The issues remaining and new issues are restated below.

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim rejections-35 USC § 101/§ 112, first paragraph

7. Claims 15-18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

This rejection is maintained for reasons of record set forth at pages 2-7 of the previous Office action (12/5/2005).

Applicants argue that "a method of detecting malignant cells by determining an amount of a protein produced by the cells, is a well established utility that is specific, substantial and credible. The utility is specific in that the specification discloses that GDF-12 is specifically expressed by liver cells and, therefore, provides a specific marker for liver cells (see, for example, Figure 1). The utility also is substantial in that there is a real world value in providing a means to determine whether an abnormal amount of liver cell proliferation is occurring in a subject, as can happen, for example, in a subject with a hepatoma or a hepatocarcinoma. Furthermore, the utility is credible because one skilled in the art would believe, for example, that an increased level of GDF-12 expression in liver cells would be associated with abnormal liver cell proliferation and malignancy because increase liver cell proliferation would be expected to produce more GDF-12."

However, contrary to Applicants arguments, the Office Action has never brought into question the credibility of the asserted utilities. However, an asserted utility must meet the three-pronged test of being credible, specific and substantial. None of the asserted utilities satisfy all three prongs. Applicants have demonstrated that the instant GDF-12 is expressed in normal liver cells. Applicants have failed to show differential expression of the GDF-12 protein in normal liver cells and in malignant liver cells. Therefore, the skilled artisan would have to conduct significant further research to determine the particular expression of the instant GDF-12 protein in malignant cells (see instant claim 15) relative to normal liver cells.

Furthermore, Applicants argue that "the level of prostate-specific antigen (PSA) in the blood was well recognized as a diagnostic marker of a prostate cell proliferative disorder, even though the function of PSA was not known. Thus, even where the function of a protein such as

PSA was not known, it was recognized that the level of PSA was increased above normal in benign prostate hyperplasia and in prostate carcinoma, presumably due, at least in part, to the increased number of prostate cells associated with these conditions and, therefore, that the levels of PSA can be indicative of a prostate cell proliferative disorder. Accordingly, Applicants submit that in the present case, one skilled in the art, viewing the specification and having knowledge of the art, would have known, for example, that increased levels of GDF-12 can be indicative of a liver cell proliferative disorder such as a hepatoma because GDF-12 is produced by liver cells and because it has been shown that increased levels of PSA, which is produced by prostate cells, is indicative of a prostate cell proliferative disorder." However, contrary to Applicants arguments, with respect to the instant GDF-12, Applicants have failed to demonstrate that GDF-12 is expressed at elevated levels in liver cancer cells. Furthermore, PSA is exclusively present in normal prostatic tissue and in benign prostatic hypertrophy and monitoring serum PSA concentrations by serial measurement is useful for the detection of residual or recurrent tumor after primary treatment and for the evaluation of response to systemic treatment of advanced disease, because PSA is exclusive to the prostate. There is no demonstration in the instant specification that GDF-12 levels are increased or even present in liver cancer cells and therefore, even an implicit disclosure of the claimed subject matter as a marker to liver cells metastasis would not be recognized by one of skill in the art from the disclosure of the instant specification.

Applicants are arguing exclusive and tissue-specific expression of GDF-12 in the liver. Therefore, the claimed antibodies cannot be used to detect all malignant cells (as recited in claim 15). Furthermore, contrary to Applicants arguments, the issue here is that at the time of filing of the instant invention, one of skill in the art, from the disclosure of the instant specification

would fail to recognize the utility of the claimed antibodies to GDF-12 as a marker for malignant cells. Applicants have not demonstrated a nexus between GDF-12 expression being upregulated in malignant cells or malignant liver cells. Therefore, the asserted utility of using GDF-12 antibodies to detect malignant cells or malignant liver cells, fails to satisfy the three-pronged test for utility: credible, specific and substantial, because there is no disclosure in the instant specification suggesting that GDF-12 expression is elevated in malignant cells.

Claim rejections-35 USC § 112, first paragraph

8. Claims 15-18 are also rejected under 35 U.S.C. 112, first paragraph.

This rejection is maintained for reasons of record set forth at page 7, of the previous Office action (12/5/2005).

Specifically, since the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim rejections-35 USC § 112, second paragraph-new rejection

9. Claims 15-18 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is rejected as vague and indefinite for several reasons.

Claim 15 recites the limitation "the sample" in line 5. There is insufficient antecedent basis for this limitation in the claim.

Claim 15, line 1, is vague and indefinite because it recites "malignant cells". It is unclear which types of malignant cells are encompassed by the claim, especially since claim 16 recites that the malignant cells are "liver cells".

Claims 16-18 are rejected as vague and indefinite insofar as they depend on rejected claim 15 for their limitations.

Conclusion

No claim is allowed.

Claims 15-18 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D., J.D.
Primary Examiner
Art Unit 1646
May 21, 2006